UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,972	07/13/2006	**Gianfranco Peluso**	1303-156	6188

23117 7590 01/09/2009

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
SHIAO, REI TSANG	
ART UNIT	**PAPER NUMBER**
1626	
MAIL DATE	**DELIVERY MODE**
01/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,972	PELUSO ET AL.	
	Examiner	Art Unit	
	REI-TSANG SHIAO	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/06, 10/21/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

ITALY MI2004A000230 with a filing date 02/12/2004.

2. Amendment of claim 1-5 and 7 in the amendment filed on October 21, 2008, is acknowledged. Claims 1-8 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statements, filed on July 13, 2006 and October 21, 2008 have been considered. Please refer to Applicant's copies of the 1449's submitted herein.

Responses to Election/Restriction

4. Applicant's election without traverse of Group I claims 1-8, in part, in the reply filed on October 21, 2008, is acknowledged. An election of a compound, i.e., R-4-trimethylammonium-3-(tetradecylcarbamoyl)-aminobutyrate, as the single species is also acknowledged.

Claims 1-8 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-8, in part, drawn to methods of use using compounds/compositions of formula (I), wherein the variables R1-R3 together with the nitrogen atom to which they are linked to do not form a heterocyclic system thereof.

Claims 1-8, embraced in above elected subject matter, are prosecuted in the case. Claims 1-8, in part, not embraced in above elected subject matter, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and therefore is made FINAL.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of formula (I) for treating leukemia or heptocarcinoma, does not reasonably provide enablement of methods of use treating any tumors without limitation, nor does limitation of the instant preparation without limitation of "peptides" or "agents modifying the biological response", see claim 1 or 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claim 1 or 6 are drawn to intent methods of use using compounds/compositions of formula (**I**) without limitation of "tumors", "peptides" or "agents modifying the biological response"(i.e., no named tumors or compounds).

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or

preventive regimen on its face. The Web site: http://www.cancercare.on.ca/ pdfdrugs/IFOSFAMI.pdf discloses Ifosfamide for treating ovarian cancer.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming intent methods of use using using compounds of formula (I) without limitation of "tumors", "peptides" or "agents modifying the biological response"(i.e., no named tumors or compounds). As such, the specification fails to enable the skilled artisan to use the compounds of claims effective to "treat tumors" without limitation (i.e., no named cancer) or no limitation of "peptides" or "agents modifying the biological response"(i.e., no named compounds).

In addition, there is no established correlation between *in vitro* or in *vivo* activity and accomplishing treatment of "treating tumors" without limitation (i.e., no named cancer) no limitation of "peptides" or "agents modifying the biological response"(i.e., no named compounds), and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use compounds of formula (I) since there is no description of an actual method wherein "treating tumors" without limitation in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of formula (I) of claim 1 due to the unpredictability of

the "treating tumors" without limitation (i.e., no named cancer). The "treating tumors" without limitation (i.e., no named cancer) and no limitation of "peptides" or "agents modifying the biological response"(i.e., no named compounds) are known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of named compounds of formula (I) for treating leukemia or heptocarcinoma, Examples 1-4 on pages 7-13 of the specification. There are no *in vitro* or *in vivo* working examples present for the treatment of any tumors without limitation and no limitation of of "peptides" or "agents modifying the biological response" by the administration of the instant invention.

The breadth of the claims

The breadth of the claims is methods of use of using the instant compounds/compositions of formula (I) effective to "treating tumors" without limitation (i.e., no named cancer) and no limitation of "peptides" or "agents modifying the biological response" (no named compounds).

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what "treating tumors" or "peptides" or "agents modifying the biological response" without limitation would be benefited (i.e., treated) by the administration of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of a disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is to practice the claimed invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment of the many tumors, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by incorporation of the named tumors (e.g., leukemia or heptocarcinoma) into claim 1 or incorporation of the named compounds of or "peptides" or "agents modifying the biological response" into claim 6 would obviate the rejection. It is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims for the "treating tumors" without limitation or "peptides" or "agents modify the biological response" without limitation.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

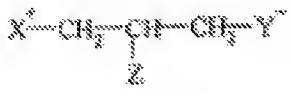
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

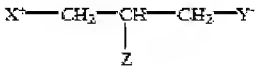
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glannessi et al. US 6,444,701 in view of Zhou et al. publication, Cancer Research, 2003, 63:7330-7337.

Applicants claim methods of use (i.e., treating tumors) using compounds of the formula (I), i.e.,  , wherein the variable Z represents –OR4, the variable X+ represents P+(R1, R2, R3) or N+(R1, R2, R3), see claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)

Glannessi et al. discloses methods of use (i.e., treating a subject having hyperactive carnitine palmitoyl-transferase) using a compound of formula (I), i.e.,



, wherein the variable Z represents –OR4, the variable X+ represents P+(R1, R2, R3) or N+(R1, R2, R3), see columns 2-3 and 34 and 42 (i.e., lines 39-41).

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Glannessi et al. is that Glannessl et al. is silent on the scope of treating tumors of the instant invention.

Zhou et al. disclose inhibitors (e.g., C75 or C273) of carnitine palmitoyl-transferase are agents for treating cancer (i.e., tumors). Glannessl et al. methods of use inherently overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 1-8 prima facie obvious **because** one would be motivated to employ the methods of use using compounds of Glannessi et al. to obtain the instant methods of use, wherein compounds of the formula (I) are used for treating tumors (i.e., leukemia or heptocarcinoma). Dependent claims 2-8 are also rejected along with claim 1 under 35 U.S.C. 103(a).

The motivation to obtain the claimed compounds/compositions derives from Glannessi et al. methods of use using similar compounds would possess similar activity (i.e., treating tumor or leukemia) to that which is claimed in the reference.

Claims Objection

7. Claims 1-8 are objected to as containing non-elected subject matter, i.e., R1-R3 together with the nitrogen atom to which they are linked form a heterocyclic system, tetrazole, morpholinium, pyridinium, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the pages 2-3 *supra*.

8. Claims 1 and 6-8 are objected to because of the following informalities:

Claim 1 is drawn to method of use claim with superfluous preamble "for the preparation of an antitumor medicament", lines 14 on page 3. Elimination of the term

"for the preparation of an antitumor medicament" would obviate the objection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from

the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Rei-tsang Shiao, Ph.D.
Primary Patent Examiner
Art Unit 1626

January 06, 2009